

US Serial No. 09/938,689
Page 2

IN THE CLAIMS:

1. (Cancelled)

2. (Cancelled)

3. (Cancelled)

4. (Cancelled)

5. (Cancelled)

6. (Cancelled)

7. (Cancelled)

8. (Cancelled)

9. (Cancelled)

10. (Cancelled)

11. (Cancelled)

12. (Cancelled)

13. (Cancelled)

14. (Cancelled)

15. (Cancelled)

US Serial No. 09/938,689
Page 3

16. (Cancelled)

B

17. (Currently Amended) A recipient mouse comprising:
a disruption in both alleles of a gene, wherein said gene modulates VDJ recombination and furthermore such that lymphocyte maturation does not occur; and
a human transgene comprising a nucleic acid sequence that encodes a MHC Class II DR3 molecule, wherein the transgene comprises naturally linked DRab and DQab alleles, wherein said transgene is incorporated into the genome of said recipient mouse; and further wherein said recipient mouse is immunodeficient and further comprises a mutation in the I-A β gene.

18. (Cancelled)

19. (Currently Amended) The mouse of claim ~~18~~ 17, wherein the gene is a RAG gene.

20. (Original) The mouse of claim 19, wherein said mouse is deficient for murine I-E α .

21. (Original) The mouse of claim 17, wherein the transgene further comprises a human HLA DQ2 gene.

22. (Currently Amended) A method of making a recipient mouse, said method comprising:
disrupting both alleles of a gene, wherein said gene modulates VDJ recombination and furthermore such so that lymphocyte maturation does not occur; and
inserting a human transgene comprising a nucleic acid sequence that encodes MHC Class II DR3 and DR3 molecule, wherein the DRab

US Serial No. 09/938,689
Page 4

and DQab alleles are naturally linked, wherein said transgene is incorporated into the genome of said recipient mouse;
inactivating murine I-E α and I-A β ; and further
wherein said recipient mouse is immunodeficient.

23. (Cancelled)

24. (Currently Amended) The method of claim 22 ~~23~~, wherein said gene is RAG-2.

B¹
25. (Original) The method of claim 24, wherein said transgene is in an artificial yeast chromosome.

26. (Original) The method of claim 25, wherein the transgene is about 550 kb in length.

27. (Original) The method of claim 26, wherein the artificial yeast chromosome is 4D1.

28. (Currently Amended) The A method of making a recipient mouse of Claim 22, wherein said method comprises:

preventing VDJ recombination by mutating both alleles of the RAG-2 gene;

inserting a transgene comprising the Drab DRab and DQab alleles of the MHC Class II DR3 haplotype;

and inactivating murine I-E α and I-A β .

29. (New) The mouse of Claim 17, wherein said mouse further comprises a disruption in both alleles of at least one gene selected from the group consisting of the RAG-1 gene, RAG-2 gene, T-cell receptor gene, and an immunoglobulin gene.

US Serial No. 09/938,689
Page 5

30. (New) The mouse of claim 29, wherein the transgene further comprises a human HLA DQ2 gene.

31. (New) The mouse of claim 29, wherein said gene is a RAG gene.

32. (New) The mouse of claim 29, wherein said mouse is deficient for murine I-E α .

B' 33. (New) The mouse of Claim 29, wherein said mouse comprises the genotype 4D1/C2D/RAG-2/I-A β °.

34. (New) A recipient mouse comprising: a disruption in both alleles of a gene, wherein said gene modulates VDJ recombination and furthermore such that lymphocyte maturation does not occur, and a human transgene comprising a nucleic acid sequence that encodes a MHC Class II molecule, wherein the transgene comprises naturally linked DR α b and DQ α b alleles, wherein said transgene is incorporated into the genome of said recipient mouse; and further wherein said recipient mouse is immunodeficient.

35. (New) The mouse of Claim 34, wherein said mouse further comprises a disruption in both alleles of at least one gene selected from the group consisting of the RAG-1 gene, RAG-2 gene, T-cell receptor gene, and an immunoglobulin gene.

36. (New) The mouse of Claim 34, wherein said transgene further comprises a human HLA DQ2 gene.

37. (New) The mouse of Claim 35, wherein said gene is a RAG gene.

38. (New) The mouse of Claim 34, wherein said mouse is deficient for murine I-E α .

US Serial No. 09/938,689
Page 6

39. (New) The mouse of Claim 34, wherein said mouse comprises the genotype 4D1/C2D/RAG-2/I-A β .

*By
att. 10*